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AN INQUIRY INTO A CHARACTERISTIC ORGANISM OF DIPHTHERIA.

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IN my communication to the *Medical Press and Circular* of the 31st ult., I made a very brief and passing reference to an early paper of mine published in the *Lancet*, March, 1873, on "the Relations of the Diphtheritic and Croupous Membranes." With your permission I propose to return to the subject, and enter more fully into the question which naturally agitates the minds of bacteriologists, the discovery of the specific germ of diphtheria. It is needless to say that, at the above-mentioned period, from the constantly recurring fungi, micro-organisms, in diphtheritic membranes, I was much inclined to believe that at no distant date a characteristic organism of this infective disease would be discovered. But although pathologists have diligently sought it, it has up to the present succeeded in eluding their grasp. Quite recently, however, we hear from German and French sources, that the specialised bacillus of diphtheria has at length been actually grasped, and will in future take its place by the side of those we already are familiar with.

Before proceeding to discuss this discovery it will be instructive to note the general unwillingness of the profession to admit a pathological difference between diphtheria and croup. In 1873, when I was an active member of the Pathological Society, the etiology, as well as the pathology, of membranous throat affections were in a very undetermined state. This fact became first apparent when, in the years 1858-59, an alarming epidemic visitation of diphtheria spread over London, and extended to some parts of the country. I well remember the prevailing lack of knowledge displayed by members of the Society who ventured to exhibit morbid specimens of the disease and show sections under the microscope. An instance or two will serve to illustrate this. In one case, the specimen shown was said to be "a false membrane made up of network of fibrillated lymph, in which epithelium was entangled." In another case the membrane was said to "consist of a delicate film, in which quantities of cells and granules were entangled, but nothing like a fibrillated structure could be found." The contradiction involved in these and numerous other very similar statements of the kind can only be explained on the supposition, that very different forms of disease were passing under review. But at that time we were taught to believe that diphtheria and croup were separated only by "clinical tradition," and "that croup accompanied by a false membrane in the larynx and trachea, is always a diphtheria, whether in the child or adult." These views I need hardly say are now quite exploded, and the great advances made in pathological anatomy of late have greatly increased our knowledge of all diseases. I refer to them merely by way of earmarking a period in medical history. We are moving onwards with the rapidity of modern inventions. Quite lately the Local Government Board backed up the Asylums Board in a peremptory notice to the effect that in future "diphtheria and membranous croup," must find a place among dangerous infective disorders which it would be the duty of officers of health to see cases of either removed from the family circle. This is no doubt as far as diphtheria is concerned a step in the right direction, but in my opinion it would be more in accord with the pathological relations of the two diseases mentioned, if the term croup, which after all is but a symptom common to other throat affections, had been abandoned, and that of membranous laryngitis substituted in its place; as herein lies the clinical difference of a previous age. There were few exceptions twenty or more years ago to the views then pretty generally accepted. The late Sir William Gull was a noteworthy exception, for in a letter of thanks for a copy of my pamphlet, he writes: "I am on all grounds glad to receive your paper on croupous and diphtheritic membranes. I have on clinical grounds always regarded the confusion of croup proper with diphtheria as a pernicious error; the two maladies have little in common besides the most superficial features." Sir James Paget believed that the typical forms of membranous throat disease were the fibrinous and the corpuscular.

The two diseases certainly widely differ in very many respects, not only etiologically but pathologically. The object I have more immediately in view is that of showing the broad line which separates the two diseases, and it will serve my purpose if I cite one or two generally-excepted features of each. Diphtheria is epidemic and endemic, and it attacks persons of all ages. Croup proper is essentially sporadic and non-contagious, usually met with in early life, that is during childhood. The combination of symptoms and associated pathological changes are so very different, that in my opinion, their nomenclature should be equally distinctive. It would, therefore, be in many ways more convenient to designate one diphtheritic membranous laryngitis, the other simply croupous laryngitis; the membrane in connection with the latter, by the way, seldom if ever is seen to extend to the pharynx, while that of diphtheria usually commences about the pharynx and often extends down to the œsophagus, and is truely a specific febrile disease of a very contagious nature. It is perhaps further removed from croup by its liability to take on dangerous combinations, of the renal functions for instance, the outcome of an induced specific morbid state of the blood.

I more particularly now desire to direct attention to the pathological changes observed in the diphtheritic membrane, but which I have already given in detail in the pamphlet referred to by Sir W. Gull. (*a*) My investigations at that time conclusively show that we had two typical forms of disease to deal with, a fibrinous and a corpuscular, and between which all similar inflammatory exudations of the throat were but intermediate. Diphtheritic membranous laryngitis undoubtedly partakes of the fibrinous, while the croupous membrane is, for the most part, corpuscular. This will at once be seen in the accompanying drawings made in 1873, and which I reproduce without alteration of any kind. The naked eye appearances present a marked contrast while the histological characteristics of the two membranes are well accentuated. The felt-like false membrane of diphtheria which is with difficulty detached during the life of the patient, invariably leaves behind a bleeding surface, even should it not have already extended to the larynx. On making a section of the exudation, and carefully teasing ti out for examination under a power of 350 diameters, it is at once seen to be made up of a network of connective tissue, elastic and non-elastic fibres, in the meshes of which are entangled layers of altered epithelium cells, blood corpuscles, fat cells, and numerous foreign bodies,

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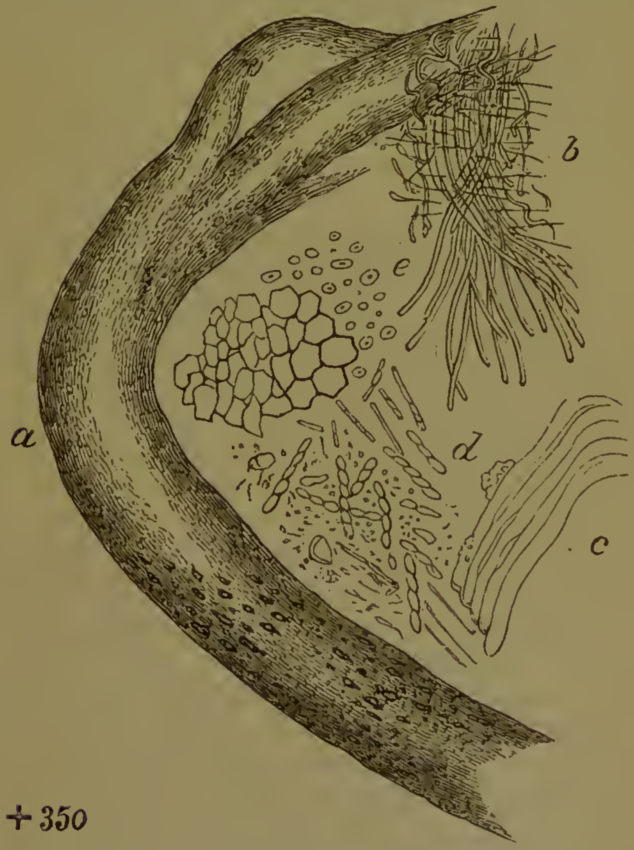
(*a*) See my paper on "The Pathological Relations of the Diphtheritic and Croupous Membranes," published originally in the "Transactions of the Medical Microscopical Society," London, June 20th, 1873.

conspicuous among which are starch granules, or other particles of food and fungi. The membrane is undoubtedly a true fibrinous exudation, a laminated fibroid tissue embracing superficial and deeper seated structures. The open mouth is apparently a natural trap of micro-organisms, and it would be difficult to say

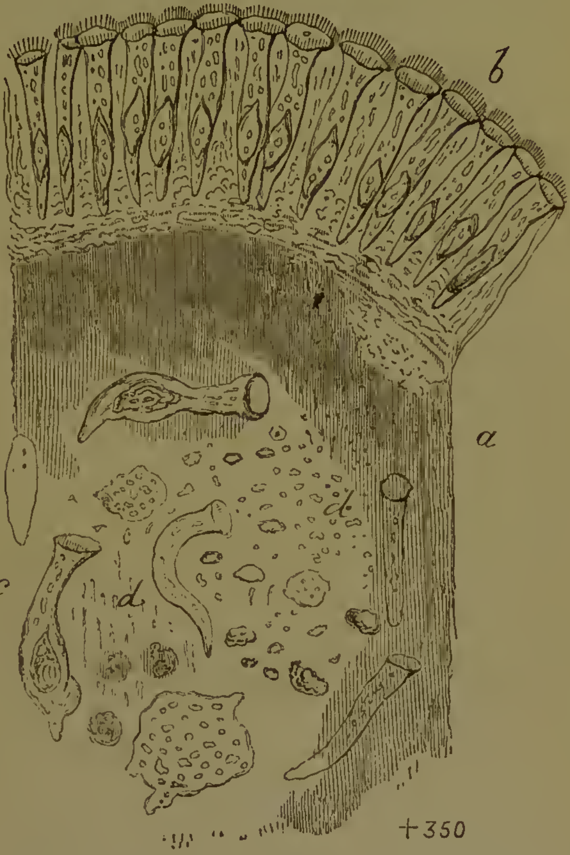


SECTION OF A DIPHTHERITIC MEMBRANE.

a. Vertical section magnified +50.
b. Connective fibrinous-tissue teased out + 350.
c. Involuntary muscular fibres.
d. Leptothrix filaments, bacilli and micrococci.
e. Epithelium cells and muco-purulent corpuscles

how far these are either an accidental or potential agency in the inflammatory processes of the mouth and throat. The filamentous "*leptothrix buccalis*" was, as is well known, discovered in the secretions of the mouth upwards of two centuries ago by a Dutch naturalist, and since double staining came into use as a differentiating aid to the more perfected modern miscroscope I have invariably found in diphtheritic and croupous membranes distinctive forms of micro-organisms, bacteria, bacilli, spirilla, and micrococci, but I cannot undertake to say whether I have met with the special bacillus, or virus of diphtheria. I am rather inclined to the view that "a characteristic bacillus" of the disease has yet to be discovered. I think I am right in saying that the majority of bacteriologists are as undecided as myself on this particular point.

The opinion generally held is that the micro-organisms found in connection with the diphtheritic membrane are common to, and indistinguishable from, those found in other forms of disease, as erysipelas, pyæmia, variola, and tuberculosis. I quite recently met with an ardent searcher after specific germs, who, in despair of finding that of diphtheria, had fallen back upon the entirely exploded doctrine of origin *de novo*, in other words, of the spontaneous generation theory of infection. If, however, continental observers—and it has now become a fashion that every discovery should emanate from Germany—have succeeded in separating the specific bacillus, and thereby communicating the disease to the lower animals, I still feel inclined to wait for corroborative evidence, and be sure that death has not been brought about by other causes, as that of the formation of a chemical product, a toxine, ptomaine, or of some such complex pathogenic substance as that of snake poison accidentally mixed in the injected fluid. With reference to this point, I observe that many of the smaller animals experimented on seem to be "immune," insusceptible of the diphtheritic poison. Cats, however, may be considered to offer an exception, as an outbreak of diphtheria has, it is said, been traced to this domestic pet. On the other



SECTION OF A CROUPOUS MEMBRANE.

a. Homogeneous matrix in which altered epithelium cells, granular and fatty matters are seen entangled.
b. Columnar epithelium with cilia retained.
c. Detached epithelium, fat and mucous corpuscles.
d. Bacilli and micrococci.

hand fungi, of some form or other, are almost invariably associated with the more delicate superficial croupous membrane. On placing a portion of a cast removed from the throat of a child, under the microscope, it is found to be chiefly made up of cylindrical and pavement epithelium cells, fat corpuscles, foreign matters, and micro-organisms, the latter being seldom entirely absent. The columnar epithelium cells remain *in situ* fringed by their cilia, and if the membrane be immediately transferred without much disturbance to the warm stage of the microscope, together with the buccal secretions, a slight movement of the cilia will occasionally be distinctly seen. This is, I think, evidence that the membrane has been only very recently formed, and can scarcely be said to be in the toxic morbid condition of that of diphtheria. The croupous films then, be it observed, are characterised by an excessive cell proliferation, in which are entangled fungus spores and other bodies, as already pointed out, and they certainly differ very materially from the dense felt-like false membrane of diphtheritic membranous laryngitis.

Thus far my investigations of 1873 had carried me towards the discovery of a specific organism or virus of diphtheria, and it is no small matter of regret that so little has since been achieved, either in the same direction, or in that of the prevention of this fatal disease.